



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/701,870 | 11/05/2003 | Fritz Sieber | 650053.91649 | 6714 |

7590 08/25/2005

Zhibin Ren
Quarles & Brady LLP
411 East Wisconsin Avenue
Milwaukee, WI 53202-4497

| |
|----------|
| EXAMINER |
|----------|

TSAY, MARSHA M

| | |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1653

DATE MAILED: 08/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

HL

Office Action Summary

Application No.

10/701,870

Applicant(s)

SIEBER ET AL.

Examiner

Marsha M. Tsay

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 June 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2,4-17 and 20-51 is/are pending in the application.
- 4a) Of the above claim(s) 31-47 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 2,4-12 and 26-30 is/are allowed.
- 6) ☒ Claim(s) 13-17, 20-25 and 48-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

This Office Action is in response to Applicants' response received June 16, 2005. Claims 1, 3, 18-19 are canceled. Claims 31-47 are withdrawn. Claims 48-51 are new. Claims 2, 4-17, 20-30, 48-51 are currently under examination.

Priority: The benefit date is November 6, 2002, for the purpose of prior art.

Withdrawal of Objections and Rejections

The objection of claim 11 due to minor informalities is withdrawn.

The rejection of claims 18-19, 26-30 under 35 U.S.C. 112, second paragraph as being indefinite is withdrawn.

The rejection of claims 1-3, 7-14, 16-19, 21-23, 25 under 35 U.S.C. 102(b) as being anticipated by Zhang et al. (2001 Biofactors 15: 27-38) is withdrawn.

Maintenance of Objections and Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-17, 25, 48-51 are rejected again under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13, 25 recite a composition comprising Se(0) particles in an amount sufficient to kill a cancer cell or an amount sufficient to reduce the intracellular

Art Unit: 1653

glutathione level of a cell, respectively. The claims are indefinite because it is unclear what a sufficient amount is. The specification also does not provide proper support for what constitutes a sufficient amount.

Claims 14-17, 48-51 are included in this rejection because they are dependent on claim 13.

In their response, Applicants assert whether a claim is definite should be viewed from the standpoint of a skilled artisan. Applicants further assert that a skilled artisan understands and appreciates that the amount of Se(0) needed to kill cancer cells can vary depending on the particular type of cancer cell being targeted and the circumstances under which Se(0) is used. Applicants' remarks are acknowledged. The instant claims are still deemed indefinite, however, because it is not apparent from the claims nor the specification what a sufficient amount is. There are many factors to consider in determining the amount of a composition that is sufficient to kill a cell, such as the type of cancer, the type of subject, the age of the subject, and the stage of the cancer. When these factors are considered, it is apparent the specification does not provide any type of guidance or reference as to how a sufficient amount of the Se(0) composition is to be determined. Therefore, the claims are indefinite as to what amount is sufficient to kill a cancer cell or what amount is sufficient to reduce the intracellular glutathione level of a cell.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 20 is rejected again under 35 U.S.C. 102(b) as being anticipated by Zhang et al. (2001 Biofactors 15: 27-38). Zhang et al. teach the biological effects of a composition comprising nano elemental selenium that is prepared with bovine serum albumin (BSA). In Figure 5, Zhang et al. show the toxicity of paraquat in causing up to 75% cell death at 1 mM by 20 hrs. Zhang et al. teach Nano-Se protected against paraquat-induced cell death in a dose-dependent manner (p. 32, results 3.2; claim 20). It is known in the art that every cell in the body makes intracellular glutathione.

As currently amended, claim 20 is drawn to a method for sensitizing a cell to a cytotoxic agent wherein the cell is resistant to the cytotoxic agent comprising the step of treating the cell with a composition comprising Se(0) particles. Zhang et al. teach Nano-Se protected the cells from paraquat toxicity, therefore meeting the limitation of instant claim 20 wherein the cell is resistant to the cytotoxic agent. Claim 20 does not make any references to cell death; therefore, the claim is anticipated by the Zhang et al. reference.

New Objections and Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

Art Unit: 1653

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21, 24 are drawn to a method for causing a cell to die wherein the cell is resistant to a cytotoxic agent comprising the steps of treating the cell with a composition comprising Se(0) particles and exposing the cell to the cytotoxic agent. In their response, Applicants assert these claims are directed at using Se(0) to sensitize cells to other cytotoxic agents and as a result promoting the cell killing activity of these agents (p. 12). However, the language of the instant claims do not appear to agree with Applicants' explanation. As currently amended, the claims 21, 24 recite a method for causing a cell to die wherein the cell is resistant to the cytotoxic agent. It is unclear how a cytotoxic agent can induce cell death when the cell is resistant to the agent.

Claims 22-23 are included in this rejection because they are dependent on claim 21.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. (2001 BioFactors 15: 27-38) and further in view of Kuchan et al. (1992 Cancer

Art Unit: 1653

Research 52(5): 1091-1095). Zhang et al. teach the reaction rate of two forms of selenium, selenite and Nano-Se (Se(0) particles) with GSH. Zhang et al. teach the ratio of reacted GSH responded linearly to increasing Se concentrations, for both forms of selenium. In other words, the level or quantity of GSH decreased as a result of Se(0) binding to GSH. Zhang et al. do not teach an in vivo system to measure the reaction rate of Se(0) with GSH.

Kuchan et al. teach cellular selenium and glutathione in a cell culture system. Kuchan et al. teach, in Figure 2, that increasing the density of both control and selenite-treated cultures resulted in a depression in intracellular GSH (p. 1093). Kuchan et al. do not teach the incorporation of Se(0) particles in vivo.

It would have been obvious to a person having ordinary skill in the art to react Se(0) particles in vivo and therefore, reduce the level of intracellular glutathione in a cell because Zhang et al. teach Se(0) particles reduce GSH levels and Zhang et al. teach a cell culture system where a different form of selenium reduces the level of intracellular glutathione in vivo.

Claims 2, 4-12, 26-30 are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is 571-272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER